

Note that the generation of T cells and/or antibodies can also be accomplished by administering cells, preferably treated to be rendered non-proliferative, which present relevant T cell or B cell epitopes for response, such as the epitopes discussed supra.

The therapeutic approaches may also include antisense therapies, wherein an antisense molecule, preferably from 10 to 100 nucleotides in length, is administered to the subject either "nude" or in a carrier, such as a liposome, to facilitate incorporation into a cell, followed by inhibition of expression of the protein. Such antisense sequences may also be incorporated into appropriate vaccines, such as in viral vectors (e.g., Vaccinia), bacterial constructs, such as variants of the known BCG vaccine, and so forth.

Other features and applications of the invention will be clear to the skilled artisan, and need not be set forth herein. The terms and expression which have been employed are used as terms of description and not of limitation, and there is no intention in the use of such terms and expression of excluding any equivalents of the features shown and described or portions thereof, it being recognized that various modifications are possible within the scope of the invention.

We claim:

1. Isolated nucleic acid molecule which encodes a cancer associated antigen, whose amino acid sequence is identical to the amino acid sequence encoded by the nucleotide sequence of SEQ ID NO: 1, 3, 4, 8, 15, 19, 22, or 26.
2. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 1.
3. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 3.
4. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 4.
5. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 8.
6. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 15.
7. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 19.
8. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 22.
9. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO: 26.
10. Expression vector comprising the isolated nucleic acid molecule of claim 1, operably linked to a promoter.

11. Eukaryotic cell line or prokaryotic cell strain, transformed or transfected with the expression vector of claim 10.
12. Isolated cancer associated antigen comprising all or part of the amino acid sequence encoded by SEQ ID NO: 1, 3, 4, 8, 15, 19, 22 or 26.
13. Eukaryotic cell line or prokaryotic cell strain, transformed or transfected with the isolated nucleic acid molecule of claim 1.
14. The eukaryotic cell line or prokaryotic cell strain of claim 13, wherein said cell line is also transfected with a nucleic acid molecule coding for a cytokine.
15. The eukaryotic cell line or prokaryotic cell strain of claim 14, wherein said cell line is further transfected by a nucleic acid molecule coding for an MHC molecule.
16. The eukaryotic cell line or prokaryotic cell strain of claim 14, wherein said cytokine is an interleukin.
17. The eukaryotic cell line or prokaryotic cell strain of claim 16, wherein said interleukin is IL-2, IL-4 or IL-12.
18. The eukaryotic cell line or prokaryotic cell strain of claim 13, wherein said cell line has been rendered non-proliferative.
19. The eukaryotic cell line of claim 13, wherein said cell line is a fibroblast cell line.
20. Expression vector comprising a mutated or attenuated virus and the isolated nucleic acid molecule of claim 1.
21. The expression vector of claim 20, wherein said virus is adenovirus or vaccinia virus.
22. The expression vector of claim 21, wherein said virus is vaccinia virus.
23. The expression vector of claim 21, wherein said virus is adenovirus.

24. Expression system useful in transfecting a cell, comprising (i) a first vector containing a nucleic acid molecule which codes for the isolated cancer associated antigen of claim 13 and (ii) a second vector selected from the group consisting of (a) a vector containing a nucleic acid molecule which codes for an MHC or HLA molecule which presents an antigen derived from said cancer associated antigen and (b) a vector containing a nucleic acid molecule which codes for an interleukin.

25. Immunogenic composition comprising the isolated cancer antigen of claim 12, and a pharmaceutically acceptable adjuvant.

26. The immunogenic composition of claim 25, wherein said adjuvant is a cytokine, a saponin, or GM-CSF.

27. Immunogenic composition comprising at least one peptide consisting of an amino acid sequence of from 8 to 12 amino acids concatenated to each other in the isolated cancer associated cancer antigen of claim 12, and a pharmaceutically acceptable adjuvant.

28. The immunogenic composition of claim 27, wherein said adjuvant is a saponin, a cytokine, or GM-CSF.

29. The immunogenic composition of claim 25, wherein said composition comprises a plurality of peptides which complex with a specific MHC molecule.

30. Immunogenic composition which comprises at least one expression vector which encodes a peptide derived from the amino acid sequence encoded by SEQ ID NO: 1, 3, 4, 8, 15, 19, 22 or 26.

31. The immunogenic composition of claim 30, wherein said at least one expression vector codes for a plurality of peptides.

32. Vaccine useful in treating a subject afflicted with a cancerous condition comprising the isolated eukaryotic cell line of claim 13 and a pharmacologically acceptable adjuvant.

33. The vaccine of claim 32, wherein said eukaryotic cell line has been rendered non-proliferative.

34. The vaccine of claim 33, wherein said eukaryotic cell line is a human cell line.

35. A composition of matter useful in treating a cancerous condition comprising a non-proliferative cell line having expressed on its surface a peptide derived from the amino acid sequence encoded by SEQ ID NO: 1, 3, 4, 8, 15, 19, 22 or 26.

36. The composition of matter of claim 35, wherein said cell line is a human cell line.

37. A composition of matter useful in treating a cancerous condition, comprising (i) a peptide derived from the amino acid sequence encoded by SEQ ID NO: 1, 3, 4, 8, 15, 19, 22 or 26, (ii) an MHC or HLA molecule, and (iii) a pharmaceutically acceptable carrier.

38. Isolated antibody which is specific for the cancer associated antigen of claim 12.

39. The isolated antibody of claim 38, wherein said antibody is a monoclonal antibody.

40. Method for screening for cancer in a sample, comprising contacting said sample with a nucleic acid molecule which hybridizes to all or part of the molecule encoded by SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 26 and determining hybridization as an indication of cancer cells in said sample.

41. A method for screening for cancer in a sample, comprising contacting said sample with the isolated antibody of claim 38, and determining binding of said antibody to a target as an indicator of cancer.

42. Method for diagnosing a cancerous condition in a subject, comprising contacting an immune reactive cell containing sample of said subject to a cell line transfected with the isolated nucleic acid molecule of claim 1, and determining interaction of said transfected cell line with said immunoreactive cell, said interaction being indicative of said cancer condition.

43. A method for determining regression, progression of onset of a cancerous condition comprising monitoring a sample from a patient with said cancerous condition for a parameter selected from the group consisting of (i) a protein encoded by SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 26, (ii) a peptide derived from said protein, (iii) cytolytic T cells specific for said peptide and an MHC molecule with which it non-covalently complexes, and (iv) antibodies specific for said CT protein, wherein amount of said parameter is indicative of progression or regression or onset of said cancerous condition.

44. The method of claim 43, wherein said sample is a body fluid or exudate.

45. The method of claim 43, wherein said sample is a tissue.

46. The method of claim 43, comprising contacting said sample with an antibody which specifically binds with said protein or peptide.

47. The method of claim 46, wherein said antibody is labelled with a radioactive label or an enzyme.

48. The method of claim 46, wherein said antibody is a monoclonal antibody.

49. The method of claim 43, comprising amplifying RNA which codes for said protein.

50. The method of claim 49, wherein said amplifying comprises carrying out polymerase chain reaction.

51. The method of claim 42, comprising contacting said sample with a nucleic acid molecule which specifically hybridizes to a nucleic acid molecule which codes for or expresses said protein.

52. The method of claim 49, wherein said nucleic acid molecule comprises SEQ ID NO: 9, 10, 11, 12, 13, 14, 17, 18, 20, 21, 24, 25, 28 or 29.

53. The method of claim 43, comprising assaying said sample for shed protein.

54. The method of claim 43, comprising assaying said sample for antibodies specific for said protein, by contacting said sample with protein.

55. Method for diagnosing a cancerous condition comprising assaying a sample taken from a subject for an immunoreactive cell specific for a peptide derived from a protein encoded by SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 26, complexed to an MHC molecule, presence of said immunoreactive cell being indicative of said cancerous condition.

56. Composition comprising at least one peptide consisting of an amino acid sequence of from 8 to 25 amino acids concatenated to each other in the isolated cancer associated antigen of claim 12, and a pharmaceutically acceptable adjuvant.

57. The composition of claim 56, wherein said adjuvant is a saponin, a cytokine, or GM-CSF.

58. The composition of claim 56, comprising a plurality of MHC binding peptides.

59. Composition comprising an expression vector which encodes at least one peptide consisting of an amino acid sequence of from 8 to 25 amino acids concatenated to each other in the isolated cancer associated antigen of claim 12, and pharmaceutically acceptable adjuvant.

60. The composition of claim 59, wherein said expression vector encodes a plurality of peptides.

61. A method for screening for possible presence of a pathological condition, comprising assaying a sample from a patient believed to have a pathological condition for antibodies specific to at least one of the cancer associated antigens encoded by SEQ ID NOS: 1, 2, 3, 4, 8, 15, 19, 22 or 26, presence of said antibodies being indicative of possible presence of said pathological condition.

62. The method of claim 61, wherein said pathological condition is cancer.

63. The method of claim 61, wherein said cancer is melanoma.

64. The method of claim 61, further comprising contacting said sample to purified cancer associated antigen encoded by SEQ ID NO: 1, 3, 4, 8, 15, 19, 22 or 26.

65. A method for screening for possible presence of a pathological condition in a subject, comprising assaying a sample taken from said subject for expression of a nucleic acid molecule, the nucleotide sequence of which comprises SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 26, expression of said nucleic acid molecule being indicative of possible presence of said pathological condition.

66. The method of claim 65, wherein said pathological condition is cancer.

67. The method of claim 65, comprising determining expression via polymerase chain reaction.

68. The method of claim 65, comprising determining expression by contacting said sample with at least one of SEQ ID NO: 9, 10, 11, 12, 13, 14, 17, 18, 20, 21, 24, 25, 28 or 29.

69. A method for determining regression, progression of onset of a cancerous condition comprising monitoring a sample from a patient with said cancerous condition for a parameter selected from the group consisting of (i) a cancer associated antigen encoded by SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 25, (ii) a peptide derived from said cancer associated antigen,

(iii) cytolytic T cells specific for said peptide and an MHC molecule with which it non-covalently complexes, and (iv) antibodies specific for said cancer associated antigen, wherein amount of said parameter is indicative of progression or regression or onset of said cancerous condition.

70. The method of claim 69, wherein said sample is a body fluid or exudate.

71. The method of claim 69, wherein said sample is a tissue.

72. The method of claim 69, comprising contacting said sample with an antibody which specifically binds with said protein or peptide.

73. The method of claim 72, wherein said antibody is labelled with a radioactive label or an enzyme.

74. The method of claim 72, wherein said antibody is a monoclonal antibody.

75. The method of claim 69, comprising amplifying RNA which codes for said protein.

76. The method of claim 75, wherein said amplifying comprises carrying out polymerase chain reaction.

77. The method of claim 69, comprising contacting said sample with a nucleic acid molecule which specifically hybridizes to a nucleic acid molecule which codes for or expresses said protein.

78. The method of claim 69, comprising assaying said sample for shed cancer associated antigen.

79. The method of claim 69, comprising assaying said sample for antibodies specific for said cancer associated antigen, by contacting said sample with said cancer associated antigen.

80. Method for screening for a cancerous condition comprising assaying a sample taken from a subject for an immunoreactive cell specific for a peptide derived from a cancer associated antigen encoded by SEQ ID NO: 1, 2, 3, 4, 8, 15, 19, 22 or 26, complexed to an MHC molecule, presence of said immunoreactive cell being indicative of said cancerous condition.

81. An isolated nucleic acid molecule consisting of a nucleotide sequence defined by SEQ ID NO: 1, 2, 3, 8, 15, 19, 22 or 26.

82. Isolated nucleic acid molecule the complimentary sequence of which hybridizes, under stringent conditions, to the nucleotide sequence set forth in SEQ ID NO: 4, 5, 8, 15, 19, 22 or 26.

83. An isolated polypeptide comprising at least 9 consecutive amino acids set forth in SEQ ID NO: 5, 7, 16, 19, 23, 27, or 30.

84. The isolated polypeptide of claim 83, comprising at least 9 consecutive amino acids set forth in SEQ ID NO: 23 or 30.

85. The isolated polypeptide of claim 84, comprising at least 9 consecutive amino acids of the amino acid sequence set forth in SEQ ID NO: 23.

86. The isolated polypeptide of claim 85, comprising amino acids 102-111, 904-912 or 1262-1270 of SEQ ID NO: 23.

87. An isolated nucleic acid molecule which encodes the amino acid sequence of SEQ ID NO: 30.

88. An isolated nucleic acid molecule which encodes the isolated polypeptide of claim 86.

89. Expression vector comprising the isolated nucleic acid molecule of claim 88, operably linked to a promoter.

<110> Jager, Dirk
Scanlan, Matthew
Gure, Ali
Jager, Elke
Knuth, Alexander
Old, Lloyd
Chen, Yao-tseng

<120> Isolated Nucleic Acid Molecules Encoding Cancer Associated Antigens,
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ggaagagata aggcctaggg aag 23

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 cgtggtcgtg gttgctggac gcg 23

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 aagccttaga attgatggac atgcaaaactt tcaaagcaga gcctcccgag aagccatctg 480
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<211> 513

<212> PRT

<213> Homo sapiens

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Ile Glu Met Gln Lys Ser Val Pro Asn Lys Ala Leu Glu Leu Lys Asn
 35 40 45

Glu Gln Thr Leu Arg Ala Asp Glu Ile Leu Pro Ser Glu Ser Lys Gln
 50 55 60

Lys Asp Tyr Glu Glu Ser Ser Trp Asp Ser Glu Ser Leu Cys Glu Thr
 65 70 75 80

Val Ser Gln Lys Asp Val Cys Leu Pro Lys Ala Thr His Gln Lys Glu
 85 90 95

Ile Asp Lys Ile Asn Gly Lys Leu Glu Glu Ser Pro Asp Asn Asp Gly
 100 105 110

Phe Leu Lys Ala Pro Cys Arg Met Lys Val Ser Ile Pro Thr Lys Ala
 115 120 125

Leu Glu Leu Met Asp Met Gln Thr Phe Lys Ala Glu Pro Pro Glu Lys
 130 135 140

Pro Ser Ala Phe Glu Pro Ala Ile Glu Met Gln Lys Ser Val Pro Asn
 145 150 155 160

Lys Ala Leu Glu Leu Lys Asn Glu Gln Thr Leu Arg Ala Asp Gln Met
 165 170 175

Phe Pro Ser Glu Ser Lys Gln Lys Lys Val Glu Glu Asn Ser Trp Asp
 180 185 190

Ser Glu Ser Leu Arg Glu Thr Val Ser Gln Lys Asp Val Cys Val Pro
 195 200 205

Lys Ala Thr His Gln Lys Glu Met Asp Lys Ile Ser Gly Lys Leu Glu
 210 215 220

Asp Ser Thr Ser Leu Ser Lys Ile Leu Asp Thr Val His Ser Cys Glu
 225 230 235 240

Arg Ala Arg Glu Leu Gln Lys Asp His Cys Glu Gln Arg Thr Gly Lys
 245 250 255

Met Glu Gln Met Lys Lys Lys Phe Cys Val Leu Lys Lys Lys Leu Ser
 260 265 270

Glu Ala Lys Glu Ile Lys Ser Gln Leu Glu Asn Gln Lys Val Lys Trp

275	280	285
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Lys Arg Arg Asn Ala Asp Ile Leu Asn Glu Lys Ile Arg Glu Glu Leu 305 310 315 320		
Gly Arg Ile Glu Glu Gln His Arg Lys Glu Leu Glu Val Lys Gln Gln 325 330 335		
Leu Glu Gln Ala Leu Arg Ile Gln Asp Ile Glu Leu Lys Ser Val Glu 340 345 350		
Ser Asn Leu Asn Gln Val Ser His Thr His Glu Asn Glu Asn Tyr Leu 355 360 365		
Leu His Gln Asn Cys Met Leu Lys Lys Glu Ile Ala Met Leu Lys Leu 370 375 380		
Glu Ile Ala Thr Leu Lys His Gln Tyr Gln Glu Lys Glu Asn Lys Tyr 385 390 395 400		
Phe Glu Asp Ile Lys Ile Leu Lys Glu Lys Asn Ala Glu Leu Gln Met 405 410 415		
Thr Leu Lys Leu Lys Glu Glu Ser Leu Thr Lys Arg Ala Ser Gln Tyr 420 425 430		
Ser Gly Gln Leu Lys Val Leu Ile Ala Glu Asn Thr Met Leu Thr Ser 435 440 445		
Lys Leu Lys Glu Lys Gln Asp Lys Glu Ile Leu Glu Ala Glu Ile Glu 450 455 460		
Ser His His Pro Arg Leu Ala Ser Ala Val Gln Asp His Asp Gln Ile 465 470 475 480		
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 35 40 45
 Leu Thr Arg Gly Trp Gly Arg Ala Trp Pro Trp Lys Gln Ile Leu Lys
 50 55 60
 Glu Leu Asp Glu Cys Tyr Glu Arg Phe Ser Arg Glu Thr Asp Gly Ala
 65 70 75 80
 Gln Lys Arg Arg Met Leu His Cys Val Gln Arg Ala Leu Ile Arg Ser
 85 90 95
 Gln Glu Leu Gly Asp Glu Lys Ile Gln Ile Val Ser Gln Met Val Glu
 100 105 110
 Leu Val Glu Asn Arg Thr Arg Gln Val Asp Ser His Val Glu Leu Phe
 115 120 125
 Glu Ala Gln Gln Glu Leu Gly Asp Thr Val Gly Asn Ser Gly Lys Val
 130 135 140
 Gly Ala Asp Arg Pro Asn Gly Asp Ala Val Ala Gln Ser Asp Lys Pro
 145 150 155 160
 Asn Ser Lys Arg Ser Arg Arg Gln Arg Asn Asn Glu Asn Arg Glu Asn
 165 170 175
 Ala Ser Ser Asn His Asp His Asp Asp Gly Ala Ser Gly Thr Pro Lys
 180 185 190
 Glu Lys Lys Ala Lys Thr Ser Lys Lys Lys Lys Arg Ser Lys Ala Lys
 195 200 205
 Ala Glu Arg Glu Ala Ser Pro Ala Asp Leu Pro Ile Asp Pro Asn Glu
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 Pro Thr Tyr Cys Leu Cys Asn Gln Val Ser Tyr Gly Glu Met Ile Gly
 225 230 235 240
 Cys Asp Asn Asp Glu Cys Pro Ile Glu Trp Phe His Phe Ser Cys Val
 245 250 255
 Gly Leu Asn His Lys Pro Lys Gly Lys Trp Tyr Cys Pro Lys Cys Arg
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 275 280 285
 Glu Arg Ala Tyr Asn Arg
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 caaagcagag cctcccagaga ag 22

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<210> 22
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<210> 23

<211> 1341

<212> PRT

<213> Homo sapiens

<400> 23

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Val Thr Phe Leu	Val Asp Arg Lys	Cys Gln Leu Asp	Val Leu Asp Gly
35		40	45
Glu His Arg Thr	Pro Leu Met Lys	Ala Leu Gln Cys	His Gln Glu Ala
50		55	60
Cys Ala Asn Ile	Leu Ile Asp Ser	Gly Ala Asp Ile	Asn Leu Val Asp
65		70	75
Val Tyr Gly Asn	Met Ala Leu His	Tyr Ala Val Tyr	Ser Gln Ile Leu
	85	90	95
Ser Val Val Ala	Lys Leu Leu Ser	His Gly Ala Val	Ile Glu Val His
	100	105	110
Asn Lys Ala Ser	Leu Thr Pro Leu	Leu Leu Ser Ile	Thr Lys Arg Ser
	115	120	125
Glu Gln Ile Val	Glu Phe Leu Leu	Ile Lys Asn Ala	Asn Ala Asn Ala
	130	135	140
Val Asn Lys Tyr	Lys Cys Thr Ala	Leu Met Leu Ala	Val Cys His Gly
145		150	155
Ser Ser Glu Ile	Val Gly Met Leu	Leu Gln Gln Asn	Val Asp Val Phe
	165	170	175
Ala Ala Asp Ile	Cys Gly Val Thr	Ala Glu His Tyr	Ala Val Thr Cys
	180	185	190
Gly Phe His His	Ile His Glu Gln	Ile Met Glu Tyr	Ile Arg Lys Leu
	195	200	205
Ser Lys Asn His	Gln Asn Thr Asn	Pro Glu Gly Thr	Ser Ala Gly Thr
	210	215	220
Pro Asp Glu Ala	Ala Pro Leu Ala	Glu Arg Thr Pro	Asp Thr Ala Glu
225		230	235
Ser Leu Val Glu	Lys Thr Pro Asp	Glu Ala Ala Pro	Leu Val Glu Arg
	245	250	255
Thr Pro Asp Thr	Ala Glu Ser Leu	Val Glu Lys Thr	Pro Asp Glu Ala
	260	265	270
Ala Ser Leu Val	Glu Gly Thr Ser	Asp Lys Ile Gln	Cys Leu Glu Lys
	275	280	285
Ala Thr Ser Gly	Lys Phe Glu Gln	Ser Ala Glu Glu	Thr Pro Arg Glu
	290	295	300
Ile Thr Ser Pro	Ala Lys Glu Thr	Ser Glu Lys Phe	Thr Trp Pro Ala
305		310	315
Lys Gly Arg Pro	Arg Lys Ile Ala	Trp Glu Lys Lys	Glu Asp Thr Pro
	325	330	335
Arg Glu Ile Met	Ser Pro Ala Lys	Glu Thr Ser Glu	Lys Phe Thr Trp
	340	345	350
Ala Ala Lys Gly	Arg Pro Arg Lys	Ile Ala Trp Glu	Lys Lys Glu Thr
	355	360	365
Pro Val Lys Thr	Gly Cys Val Ala	Arg Val Thr Ser	Asn Lys Thr Lys
	370	375	380
Val Leu Glu Lys	Gly Arg Ser Lys	Met Ile Ala Cys	Pro Thr Lys Glu

385	390	395	400
Ser Ser Thr Lys Ala Ser Ala Asn Asp Gln Arg Phe Pro Ser Glu Ser			
	405	410	415
Lys Gln Glu Glu Asp Glu Glu Tyr Ser Cys Asp Ser Arg Ser Leu Phe			
	420	425	430
Glu Ser Ser Ala Lys Ile Gln Val Cys Ile Pro Glu Ser Ile Tyr Gln			
	435	440	445
Lys Val Met Glu Ile Asn Arg Glu Val Glu Glu Pro Pro Lys Lys Pro			
	450	455	460
Ser Ala Phe Lys Pro Ala Ile Glu Met Gln Asn Ser Val Pro Asn Lys			
	465	470	480
Ala Phe Glu Leu Lys Asn Glu Gln Thr Leu Arg Ala Asp Pro Met Phe			
	485	490	495
Pro Pro Glu Ser Lys Gln Lys Asp Tyr Glu Glu Asn Ser Trp Asp Ser			
	500	505	510
Glu Ser Leu Cys Glu Thr Val Ser Gln Lys Asp Val Cys Leu Pro Lys			
	515	520	525
Ala Thr His Gln Lys Glu Ile Asp Lys Ile Asn Gly Lys Leu Glu Glu			
	530	535	540
Ser Pro Asn Lys Asp Gly Leu Leu Lys Ala Thr Cys Gly Met Lys Val			
	545	550	560
Ser Ile Pro Thr Lys Ala Leu Glu Leu Lys Asp Met Gln Thr Phe Lys			
	565	570	575
Ala Glu Pro Pro Gly Lys Pro Ser Ala Phe Glu Pro Ala Thr Glu Met			
	580	585	590
Gln Lys Ser Val Pro Asn Lys Ala Leu Glu Leu Lys Asn Glu Gln Thr			
	595	600	605
Trp Arg Ala Asp Glu Ile Leu Pro Ser Glu Ser Lys Gln Lys Asp Tyr			
	610	615	620
Glu Glu Asn Ser Trp Asp Thr Glu Ser Leu Cys Glu Thr Val Ser Gln			
	625	630	635
Lys Asp Val Cys Leu Pro Lys Ala Ala His Gln Lys Glu Ile Asp Lys			
	645	650	655
Ile Asn Gly Lys Leu Glu Gly Ser Pro Val Lys Asp Gly Leu Leu Lys			
	660	665	670
Ala Asn Cys Gly Met Lys Val Ser Ile Pro Thr Lys Ala Leu Glu Leu			
	675	680	685
Met Asp Met Gln Thr Phe Lys Ala Glu Pro Pro Glu Lys Pro Ser Ala			
	690	695	700
Phe Glu Pro Ala Ile Glu Met Gln Lys Ser Val Pro Asn Lys Ala Leu			
	705	710	720
Glu Leu Lys Asn Glu Gln Thr Leu Arg Ala Asp Glu Ile Leu Pro Ser			
	725	730	735
Glu Ser Lys Gln Lys Asp Tyr Glu Glu Ser Ser Trp Asp Ser Glu Ser			
	740	745	750
Leu Cys Glu Thr Val Ser Gln Lys Asp Val Cys Leu Pro Lys Ala Thr			
	755	760	765
His Gln Lys Glu Ile Asp Lys Ile Asn Gly Lys Leu Glu Glu Ser Pro			

770	775	780
Asp Asn Asp Gly Phe Leu Lys Ala Pro Cys Arg Met Lys Val Ser Ile 785 790 795 800		
Pro Thr Lys Ala Leu Glu Leu Met Asp Met Gln Thr Phe Lys Ala Glu 805 810 815		
Pro Pro Glu Lys Pro Ser Ala Phe Glu Pro Ala Ile Glu Met Gln Lys 820 825 830		
Ser Val Pro Asn Lys Ala Leu Glu Leu Lys Asn Glu Gln Thr Leu Arg 835 840 845		
Ala Asp Gln Met Phe Pro Ser Glu Ser Lys Gln Lys Lys Val Glu Glu 850 855 860		
Asn Ser Trp Asp Ser Glu Ser Leu Arg Glu Thr Val Ser Gln Lys Asp 865 870 875 880		
Val Cys Val Pro Lys Ala Thr His Gln Lys Glu Met Asp Lys Ile Ser 885 890 895		
Gly Lys Leu Glu Asp Ser Thr Ser Leu Ser Lys Ile Leu Asp Thr Val 900 905 910		
His Ser Cys Glu Arg Ala Arg Glu Leu Gln Lys Asp His Cys Glu Gln 915 920 925		
Arg Thr Gly Lys Met Glu Gln Met Lys Lys Lys Phe Cys Val Leu Lys 930 935 940		
Lys Lys Leu Ser Glu Ala Lys Glu Ile Lys Ser Gln Leu Glu Asn Gln 945 950 955 960		
Lys Val Lys Trp Glu Gln Glu Leu Cys Ser Val Arg Leu Thr Leu Asn 965 970 975		
Gln Glu Glu Glu Lys Arg Arg Asn Ala Asp Ile Leu Asn Glu Lys Ile 980 985 990		
Arg Glu Glu Leu Gly Arg Ile Glu Glu Gln His Arg Lys Glu Leu Glu 995 1000 1005		
Val Lys Gln Gln Leu Glu Gln Ala Leu Arg Ile Gln Asp Ile Gln Leu 1010 1015 1020		
Lys Ser Val Glu Ser Asn Leu Asn Gln Val Ser His Thr His Glu Asn 1025 1030 1035 1040		
Gln Asn Tyr Leu Leu His Glu Asn Cys Met Leu Lys Lys Glu Ile Ala 1045 1050 1055		
Met Leu Lys Leu Glu Ile Ala Thr Leu Lys His Glu Tyr Gln Glu Lys 1060 1065 1070		
Glu Asn Lys Tyr Phe Glu Asp Ile Lys Ile Leu Lys Glu Lys Asn Ala 1075 1080 1085		
Glu Leu Gln Met Thr Leu Lys Leu Lys Glu Glu Ser Leu Thr Lys Arg 1090 1095 1100		
Ala Ser Gln Tyr Ser Gly Gln Leu Lys Val Leu Ile Ala Glu Asn Thr 1105 1110 1115 1120		
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 Asp Ile His Phe Leu Glu Arg Lys Met Gln His His Leu Leu Lys Glu
 1300 1305 1310
 Lys Asn Glu Glu Ile Phe Asn Tyr Asn Asn His Leu Lys Asn Arg Ile
 1315 1320 1325
 Tyr Gln Tyr Glu Lys Glu Lys Ala Glu Thr Glu Asn Ser
 1330 1335 1340

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 aatgggaaca agagctctgc ag 22

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 gggtcctctg aagttcagca ttc 23

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 gtaggggctg gggaaggcg agcgggaggc ggggctctc tctagcaggg ggctgcagcc 180
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 ttcagcgaac gggctctaac tgagaaggac tacgggacca tctacttcgg ggaatctagg 300
 aagatccata cagctgcctc ccggggccaa gtccagaagc tggagaagat gacagtaggg 360
 aagaagcccg tcaacctgaa caaaagagat atgaagaaga ggactgctct acactggggc 420

tgtgtcaatg gccatgcana agtagtaaca tttctggtag acagaaagt cngottaat 480
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 ttgtgcaaat attctcatag atgttggtgc tgatctaaat tatgtagatg tgtatggcaa 600
 cagggtctct cattatgccc tttatagtga gaatttatta atgggtggcaa cactgctgto 660
 ctatggtgca gtcatogagg tgcaaaacaa ggttagcctc acaccccttt tactggccat 720
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<211> 1011

<212> PRT

<213> Homo sapiens

<400> 27

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Lys Ala Ser Leu Thr Pro Leu Leu Leu Ala Ile Gln Lys Arg Ser Lys
 20 25 30

Gln Thr Val Glu Phe Leu Leu Thr Lys Asn Ala Asn Ala Asn Ala Phe
 35 40 45

Asn Glu Ser Lys Cys Thr Ala Leu Met Leu Ala Ile Cys Glu Gly Ser
 50 55 60

Ser Glu Ile Val Gly Met Leu Leu Gln Gln Asn Val Asp Val Phe Ala
 65 70 75 80

Glu Asp Ile His Gly Ile Thr Ala Glu Arg Tyr Ala Ala Ala Arg Gly
 85 90 95

Val Asn Tyr Ile His Gln Gln Leu Leu Glu His Ile Arg Lys Leu Pro
 100 105 110

Lys Asn Pro Gln Asn Thr Asn Pro Glu Gly Thr Ser Thr Gly Thr Pro
 115 120 125

Asp Glu Ala Ala Pro Leu Ala Glu Arg Thr Pro Asp Thr Ala Glu Ser
 130 135 140

Leu Leu Glu Lys Thr Pro Asp Glu Ala Ala Arg Leu Val Glu Gly Thr

145		150		155		160
Ser Ala Lys Ile	Gln Cys Leu Gly Lys	Ala Thr Ser Gly Lys	Phe Glu			
	165	170	175			
Gln Ser Thr Glu	Glu Thr Pro Arg Lys	Ile Leu Arg Pro Thr	Lys Glu			
	180	185	190			
Thr Ser Glu Lys	Phe Ser Trp Pro Ala Lys	Gln Arg Ser Arg Lys	Ile			
	195	200	205			
Thr Trp Glu Glu	Lys Glu Thr Ser Val Lys	Thr Glu Cys Val Ala	Gly			
	210	215	220			
Val Thr Pro Asn	Lys Thr Glu Val Leu Glu Lys	Gly Thr Ser Asn Met				
	225	230	235			240
Ile Ala Cys Pro	Thr Lys Glu Thr Ser Thr	Lys Ala Ser Thr Asn	Val			
	245	250	255			
Asp Val Ser Ser	Val Glu Pro Ile Phe Ser	Leu Phe Gly Thr Arg	Thr			
	260	265	270			
Ile Glu Asn Ser	Gln Cys Thr Lys Val Glu	Glu Asp Phe Asn Leu	Ala			
	275	280	285			
Thr Lys Ile Ile	Ser Lys Ser Ala Ala Gln	Asn Tyr Thr Cys Leu	Pro			
	290	295	300			
Asp Ala Thr Tyr	Gln Lys Asp Ile Lys Thr	Ile Asn His Lys Ile	Glu			
	305	310	315			320
Asp Gln Met Phe	Pro Ser Glu Ser Lys Arg	Glu Glu Asp Glu Glu	Tyr			
	325	330	335			
Ser Trp Asp Ser	Gly Ser Leu Phe Glu Ser	Ser Ala Lys Thr Gln	Val			
	340	345	350			
Cys Ile Pro Glu	Ser Met Tyr Gln Lys	Val Met Glu Ile Asn	Arg Glu			
	355	360	365			
Val Glu Glu Leu	Pro Glu Lys Pro Ser Ala	Phe Lys Pro Ala Val	Glu			
	370	375	380			
Met Gln Lys Thr	Val Pro Asn Lys Ala Phe	Gln Leu Lys Asn Glu	Gln			
	385	390	395			400
Thr Leu Arg Ala	Ala Gln Met Phe Pro Ser	Glu Ser Lys Gln Lys	Asp			
	405	410	415			
Asp Glu Glu Asn	Ser Trp Asp Ser Glu Ser	Pro Cys Glu Thr Val	Ser			
	420	425	430			
Gln Lys Asp Val	Tyr Leu Pro Lys Ala Thr	His Gln Lys Glu Phe	Asp			
	435	440	445			
Thr Leu Ser Gly	Lys Leu Glu Gln Ser Pro	Val Lys Asp Gly Leu	Leu			
	450	455	460			
Lys Pro Thr Cys	Gly Arg Lys Val Ser Leu	Pro Asn Lys Ala Leu	Glu			
	465	470	475			480
Leu Lys Asp Arg	Glu Thr Phe Lys Ala Glu	Ser Pro Asp Lys Asp	Gly			
	485	490	495			
Leu Leu Lys Pro	Thr Cys Gly Arg Lys	Val Ser Leu Pro Asn	Lys Ala			
	500	505	510			
Leu Glu Leu Lys	Asp Arg Glu Thr Leu Lys	Ala Glu Ser Pro Asp	Asn			
	515	520	525			
Asp Gly Leu Leu	Lys Pro Thr Cys Gly Arg	Lys Val Ser Leu Pro	Asn			

530	535	540
Lys Ala Leu Glu Leu Lys Asp Arg Glu Thr Phe Lys Ala Ala Gln Met 545	550	555
Phe Pro Ser Glu Ser Lys Gln Lys Asp Asp Glu Glu Asn Ser Trp Asp 565	570	575
Phe Glu Ser Phe Leu Glu Thr Leu Leu Gln Asn Asp Val Cys Leu Pro 580	585	590
Lys Ala Thr His Gln Lys Glu Phe Asp Thr Leu Ser Gly Lys Leu Glu 595	600	605
Glu Ser Pro Asp Lys Asp Gly Leu Leu Lys Pro Thr Cys Gly Met Lys 610	615	620
Ile Ser Leu Pro Asn Lys Ala Leu Glu Leu Lys Asp Arg Glu Thr Phe 625	630	635
Lys Ala Glu Asp Val Ser Ser Val Glu Ser Thr Phe Ser Leu Phe Gly 645	650	655
Lys Pro Thr Thr Glu Asn Ser Gln Ser Thr Lys Val Glu Glu Asp Phe 660	665	670
Asn Leu Thr Thr Lys Glu Gly Ala Thr Lys Thr Val Thr Gly Gln Gln 675	680	685
Glu Arg Asp Ile Gly Ile Ile Glu Arg Ala Pro Gln Asp Gln Thr Asn 690	695	700
Lys Met Pro Thr Ser Glu Leu Gly Arg Lys Glu Asp Thr Lys Ser Thr 705	710	715
Ser Asp Ser Glu Ile Ile Ser Val Ser Asp Thr Gln Asn Tyr Glu Cys 725	730	735
Leu Pro Glu Ala Thr Tyr Glu Lys Glu Ile Lys Thr Thr Asn Gly Lys 740	745	750
Ile Glu Glu Ser Pro Glu Lys Pro Ser His Phe Glu Pro Ala Thr Glu 755	760	765
Met Gln Asn Ser Val Pro Asn Lys Gly Leu Glu Trp Lys Asn Lys Gln 770	775	780
Thr Leu Arg Ala Asp Ser Thr Thr Leu Ser Lys Ile Leu Asp Ala Leu 785	790	795
Pro Ser Cys Glu Arg Gly Arg Glu Leu Lys Lys Asp Asn Cys Glu Gln 805	810	815
Ile Thr Ala Lys Met Glu Gln Met Lys Asn Lys Phe Cys Val Leu Gln 820	825	830
Lys Glu Leu Ser Glu Ala Lys Glu Ile Lys Ser Gln Leu Glu Asn Gln 835	840	845
Lys Ala Lys Trp Glu Gln Glu Leu Cys Ser Val Arg Leu Pro Leu Asn 850	855	860
Gln Glu Glu Glu Lys Arg Arg Asn Val Asp Ile Leu Lys Glu Lys Ile 865	870	875
Arg Pro Glu Glu Gln Leu Arg Lys Lys Leu Glu Val Lys His Gln Leu 885	890	895
Glu Gln Thr Leu Arg Ile Gln Asp Ile Glu Leu Lys Ser Val Thr Ser 900	905	910
Asn Leu Asn Gln Val Ser His Thr His Glu Ser Glu Asn Asp Leu Phe		

915 920 925
 His Glu Asn Cys Met Leu Lys Lys Glu Ile Ala Met Leu Lys Leu Glu
 930 935 940
 Val Ala Thr Leu Lys His Gln His Gln Val Lys Glu Asn Lys Tyr Phe
 945 950 955 960
 Glu Asp Ile Lys Ile Leu Gln Glu Lys Asn Ala Glu Leu Gln Met Thr
 965 970 975
 Leu Lys Leu Lys Gln Lys Thr Val Thr Lys Arg Ala Ser Gln Tyr Arg
 980 985 990
 Glu Gln Leu Lys Val Leu Thr Ala Glu Asn Thr Met Leu Thr Ser Lys
 995 1000 1005
 Leu Lys Glu
 1010

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 <400> 28
 tctcatagat gctggtgctg atc 23

<210> 29
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 <212> DNA
 <213> Homo sapiens
 <400> 29
 cccagacatt gaattttggc agac 24

<210> 30
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 <212> PRT
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Met Glu Glu Ile Ser Ala Ala Ala Val Lys Val Val Pro Gly Pro Glu
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 Arg Pro Ser Pro Phe Ser Gln Leu Val Tyr Thr Ser Asn Asp Ser Tyr
 20 25 30
 Ile Val His Ser Gly Asp Leu Arg Lys Ile His Lys Ala Ala Ser Arg
 35 40 45
 Gly Gln Val Arg Lys Leu Glu Lys
 50 55